

VAUTHIER
Appl. No. 10/533,084
Atty. Dkt. 5006-5
Amendment
December 23, 2008

AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Please replace the paragraph on page 4 spanning lines 5-10 and insert the following therefor:

The hydrophilic segment that is saccharide in nature is a natural or synthetic oligosaccharide or polysaccharide, that may or may not be modified, as defined in application WO 02/39979 (as translated in U.S. Published Patent Application No. 2004/0028635). It is advantageously dextran, where appropriate sulfated, or heparin.

Please add the following new paragraphs on page 4, line 11:

The segment of saccharide nature derives from an oligo- or polysaccharide of natural or synthetic origin which may or may not have been modified.

The term "modified polysaccharide" is understood to mean any polysaccharide which has undergone a change on its backbone, such as, for example, the introduction of reactive functional groups or the grafting of chemical entities (molecules, aliphatic links, PEG chains, and the like). Polysaccharides modified by grafting biotin, fluorescent compounds, and the like, are available commercially. Other polysaccharides grafted with hydrophilic chains (for example, PEG) have been described in the literature. It is also possible to envisage using, in the context of the present invention, polysaccharides modified like those described in the reference Jozefowicz and Jozefonvicz, Biomaterials, 18, 1633-1644 (1997). Of course, this modification must not affect the

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polymerization of the monomer of general formula (II) in the presence of the modified oligo- or polysaccharide.

According to a preferred alternative form of the invention, the oligo- or polysaccharide employed according to the invention may already per se possess biological properties and/or activities. For example, it may confer anticoagulant, vaccinating or targeting properties or even masking properties, to prevent capture by the macrophages of the MPS.

Thus it is that it can be:

oligo- or polysaccharides exhibiting antigenic properties, such as, for example, those of bacterial or viral origin,

oligo- or polysaccharides possessing biological activity, such as, for example, heparin, heparan sulfate, dermatan sulfate, dextran sulfate and pentosan sulfate, dextran substituted by carboxyl and sulfate or sulfonate groups, sulfated polysaccharides extracted from algae (fucans and fucoidans), poly(sialic acid)s or sulfated hyaluronic acid, which possess anticoagulant activities or antiinflammatory activities, to variable extents, and/or

oligo- or polysaccharides which are involved in cell recognition and cell signaling processes, such as, for example, poly(sialic acid)s, heparin sulfate, blood group antigens, polysaccharides and lipopolysaccharides of various bacterial strains, oligosaccharide chains of membrane and/or circulating glycoproteins, and oligosaccharide chains of glycolipids.

The polysaccharides which are very particularly suitable in the invention are or derive from D-glucose (cellulose, starch, dextran, cyclodextrin), D-galactose, D-mannose, D-fructose (galactosan, mannan, fructosan) or fucose (fucan). The majority of these polysaccharides comprise the elements carbon, oxygen and hydrogen. The polysaccharides in accordance with the invention can also comprise sulfur and/or nitrogen. They can thus derive from glycoprotein or from glycolipid. Likewise, hyaluronic acid (composed of N-acetylglucosamine and glucuronic acid units), poly(sialic acid), also known as colominic acid or poly(N-acetylneuraminic acid), chitosan, chitin, heparin or orosomucoid comprise nitrogen, while agar, a polysaccharide extracted from marine algae, comprises sulfur in the form of hydrogen sulfate ($>\text{CH}-\text{O}-\text{SO}_3\text{H}$). Chondroitin sulfuric acid and heparin comprise both sulfur and nitrogen.

According to a preferred alternative form of the invention, the polysaccharide has a molecular weight of greater than or equal to 6000 g/mol.

In the specific case of dextran and of amylose $(\text{C}_6\text{H}_{10}\text{O}_5)_n$, n varies between 10 and 620 and preferably between 33 and 220. In the case of hyaluronic acid, the molar mass varies between 5×10^3 and 5×10^6 g/mol, preferably between 5×1 and 2×10^6 g/mol. In the case of chitosan, the molar mass varies between 6×10^3 and 6×10^5 g/mol, preferably between 6×10^3 and 15×10^4 g/mol.

Mention may be made, as illustration of the polysaccharides which are more particularly suitable in the invention, of polydextroses, such as dextran, chitosan, pullulan, starch, amylose, cyclodextrins, hyaluronic acid, heparin, amylopectin, cellulose, pectin, alginate, curdlan, fucan, succinoglycan, chitin, xylan, xanthan,

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arabinan, carrageenan, poly(glucuronic acid), poly(N-acetylneuraminic acid), poly(mannuronic acid) and their derivatives (such as, for example, dextran sulfate, amylose esters, cellulose acetate, pentosan sulfate, and the like).

Dextran, heparin, poly(N-acetylneuraminic acid), amylose, chitosan, pectin and hyaluronic acid, and their derivatives, are more particularly preferred.